Nervous System Neoplasm

BIO392 Project Presentation

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Introduction

- Nervous System Neoplasm = Brain tumors + Spinal tumors
- Among the most fatal cancers in adults as well as children and adolescents
- Symptoms: Headache, nausea, partial loss of sensory and motor function

Classification:

- Spinal cord tumors
- Peripheral Nerve tumors
- Meningiomas
- Brain tumors
  - Gliomas and Ependymomas
    - Astrocytomas
    - Oligodendrogliomas
   - Glioblastomas
  - Medulloblastomas

Aim

- Does survival differ among different subtypes of Nervous System Neoplasms?
- How do copy number variations in four genes of interest affect survival?
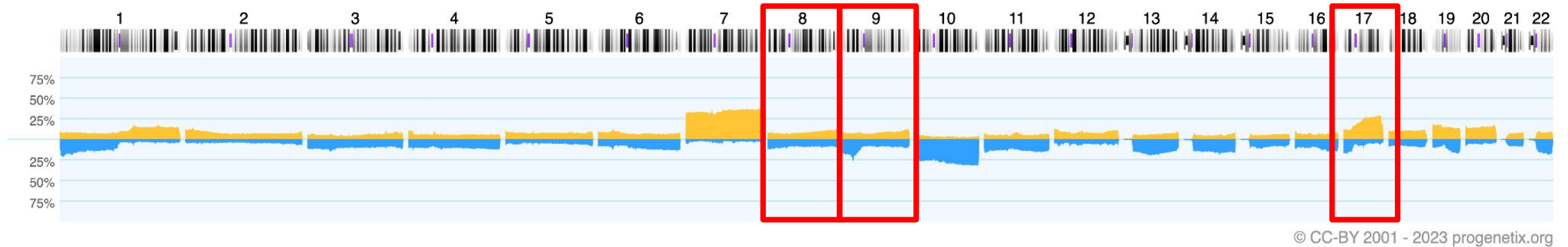- Are there differences in survival between male and female patients?

Genome wide look

Locations

- MYC: 8q24.21
- CDKN2A: 9p21.3
- ERBB2: 17q12
- TP53: 17p13.1

NCIT:C3268: Nervous System Neoplasm (15770 samples)
Chromosome 17

TP53   ERBB2
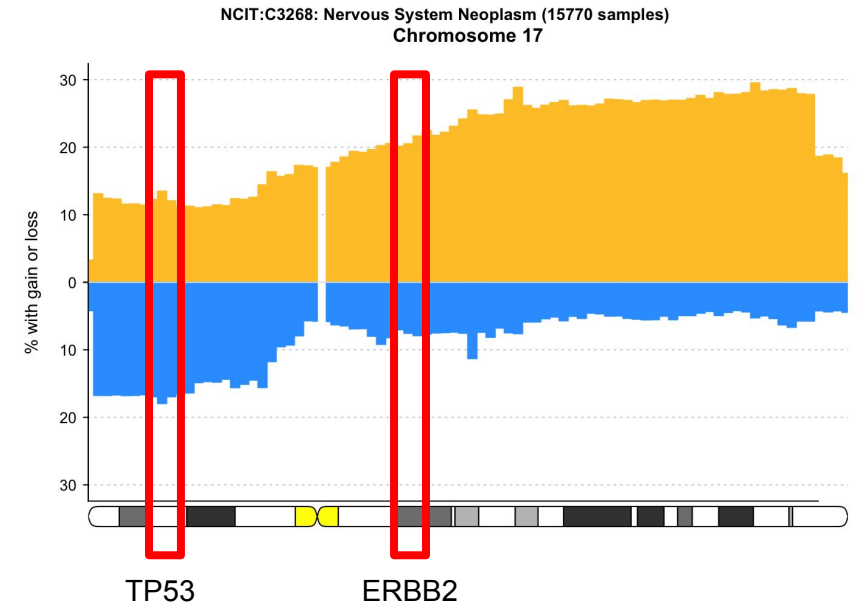
Nervous System Neoplasm (NCIT:C3268)
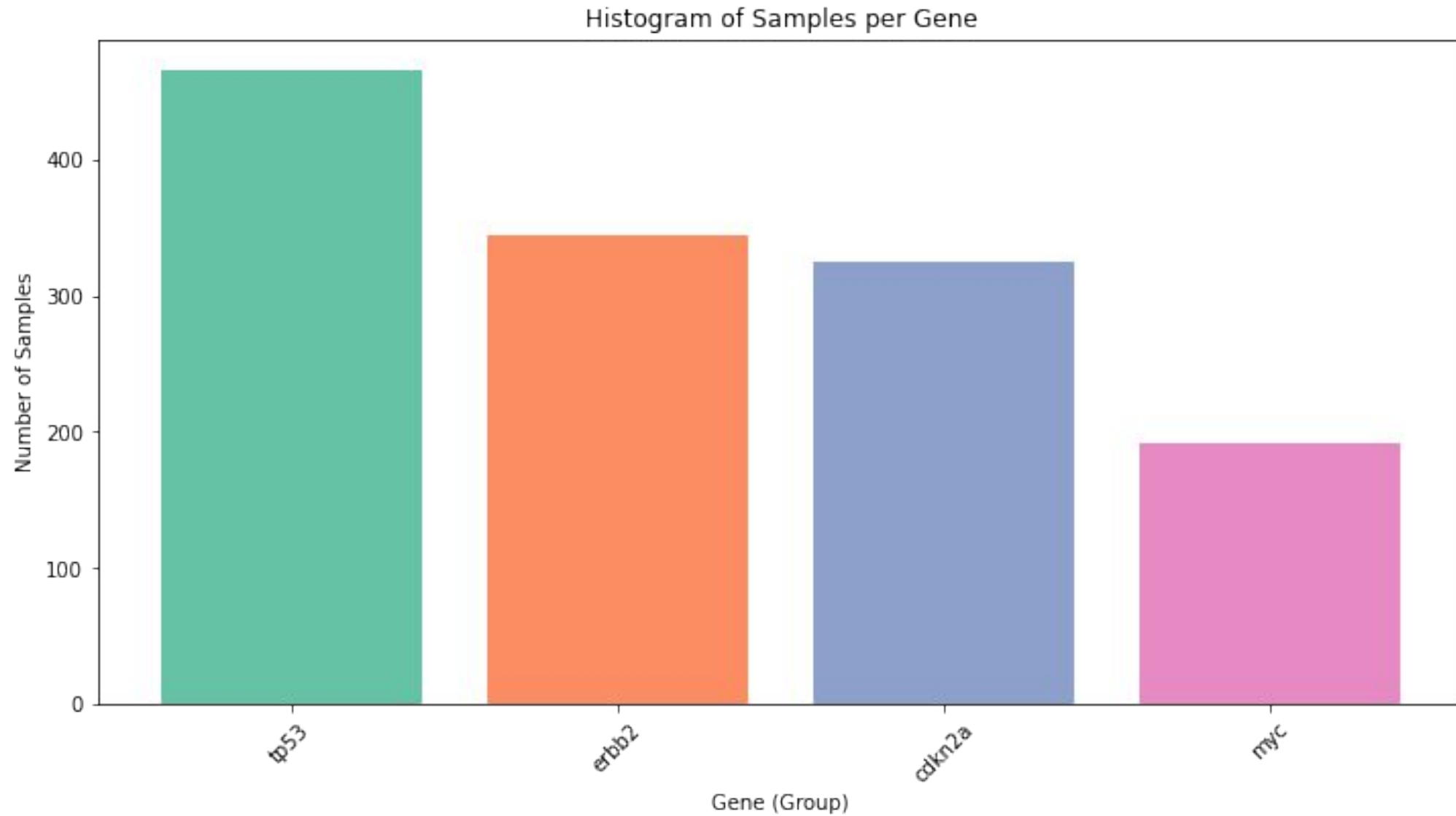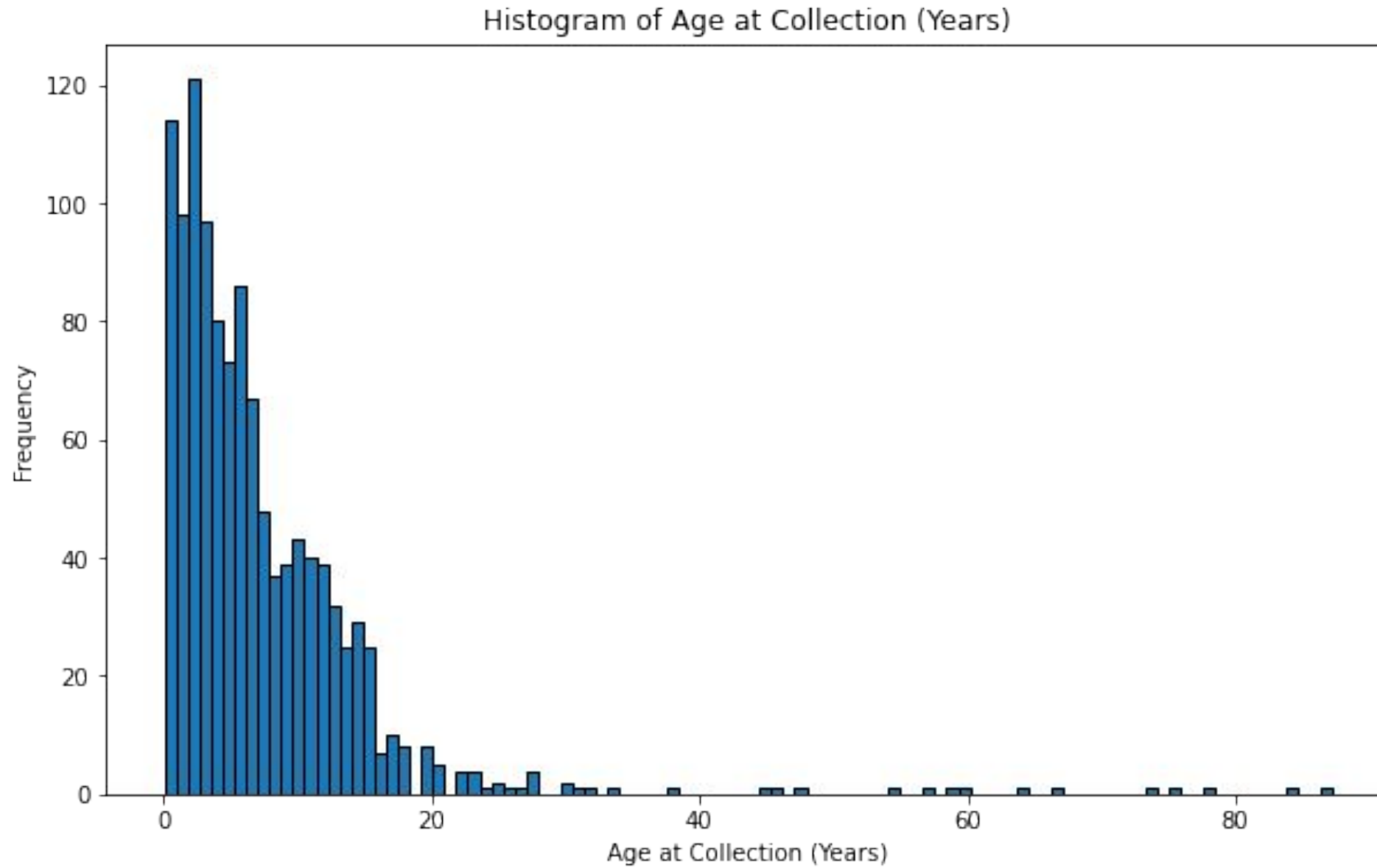
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Data

- 2560 biosamples
- 26 cancer types, histologically classified
- CN variation data from progenetix.org
- Focus:
  - Duplications in oncogenes (MYC, ERBB2)
  - Deletions in tumor suppressor genes (TP53, CDKN2A)
- 1325 samples after merging

Glioblastoma	706
Neuroblastoma	521
Medulloblastoma	424
Ependymoma	164
Desmoplastic/Nodular Medulloblastoma	97
Large Cell Medulloblastoma	74
Primitive Neuroectodermal Tumor	61
Astrocytoma	56
Malignant Glioma	52
Central Nervous System Embryonal Tumor, Not Otherwise Specified	52
Mixed Glioma	48
Retinoblastoma	46
Malignant Peripheral Nerve Sheath Tumor	46
Oligodendroglioma	35
Atypical Choroid Plexus Papilloma	32
Anaplastic Ependymoma	30
Gliomatosis Cerebri	23
Myxopapillary Ependymoma	18
Choroid Plexus Carcinoma	13
Atypical Teratoid/Rhabdoid Tumor	13
Gliosarcoma	12
Olfactory Neuroblastoma	12
Pineoblastoma	10
Ganglioneuroblastoma	7
Pleomorphic Xanthoastrocytoma	4
Fibrillary Astrocytoma	4

Data

Histogram of Samples per Gene

Data

Histogram of Age at Collection (Years)

Data

Boxplot of CNV Fraction per Group
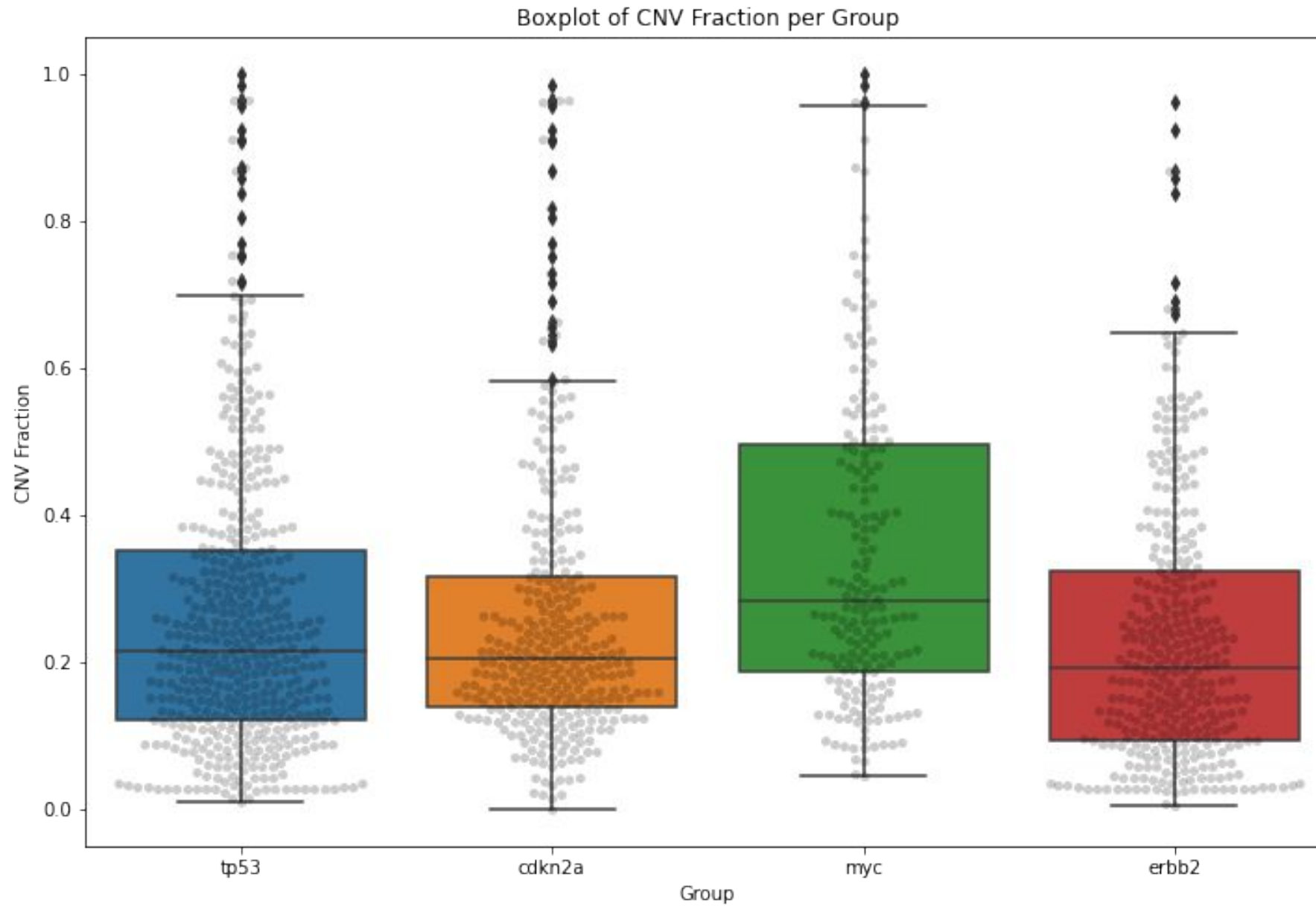
Results

Survival times for all cancers

Logrank P-Value = nan

Legend:
- Desmoplastic/Nodular Medulloblastoma (26/45)
- Ependymoma (62/98)
- Glioblastoma (195/379)
- Large Cell Medulloblastoma (46/101)
- Malignant Peripheral Nerve Sheath Tumor (21/98)
- Medulloblastoma (208/368)
- Neuroblastoma (25/41)
- Primitive Neuroectodermal Tumor (5/34)

Axes: Survival function vs Time (Months)
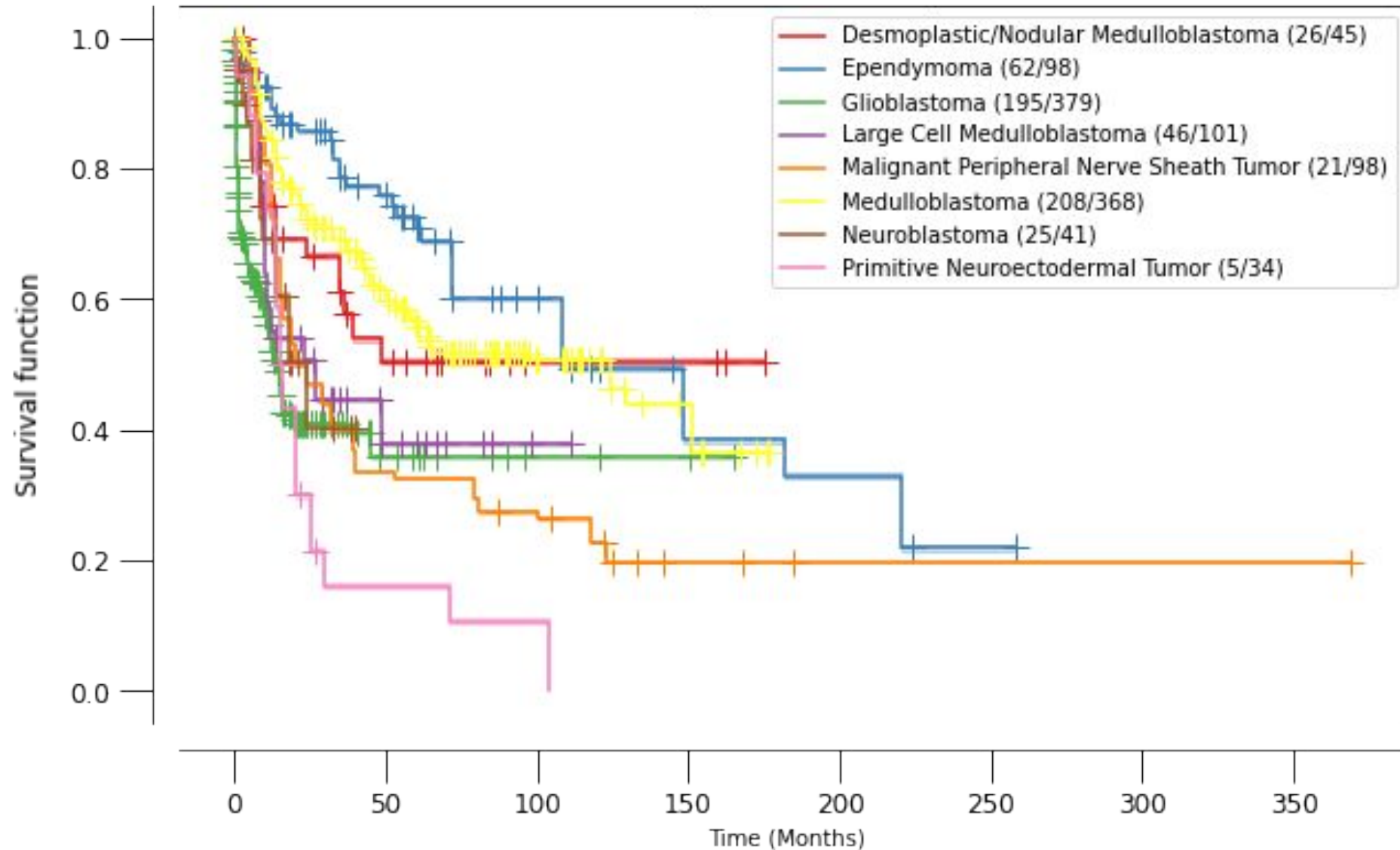
Results

Survival times for all cancers stratified per gene

Logrank P-Value = nan

Legend:
- cdkn2a (143/324)
- erbb2 (182/344)
- myc (90/192)
- tp53 (251/465)

Results
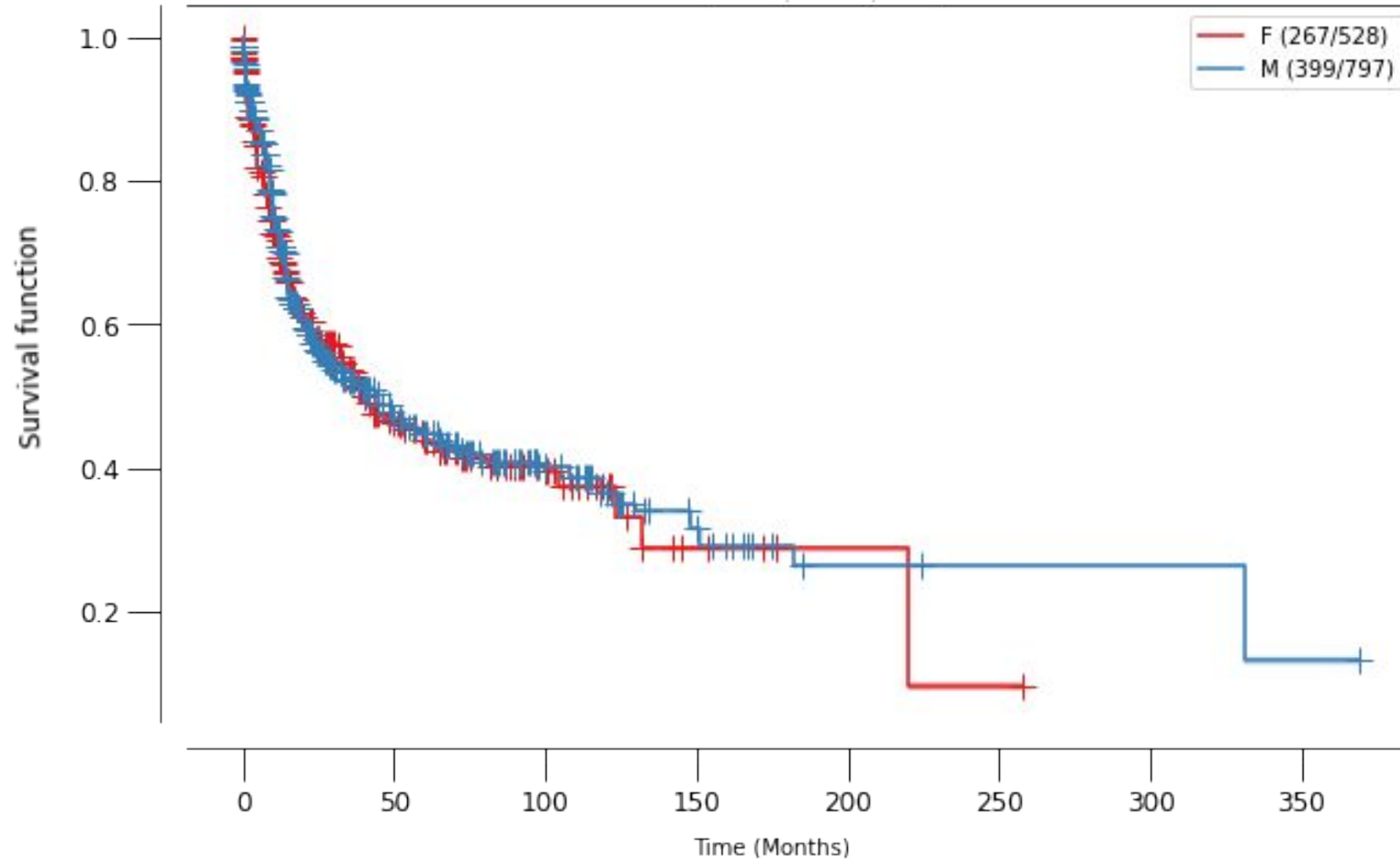

Glioblastoma survival times stratified per gene
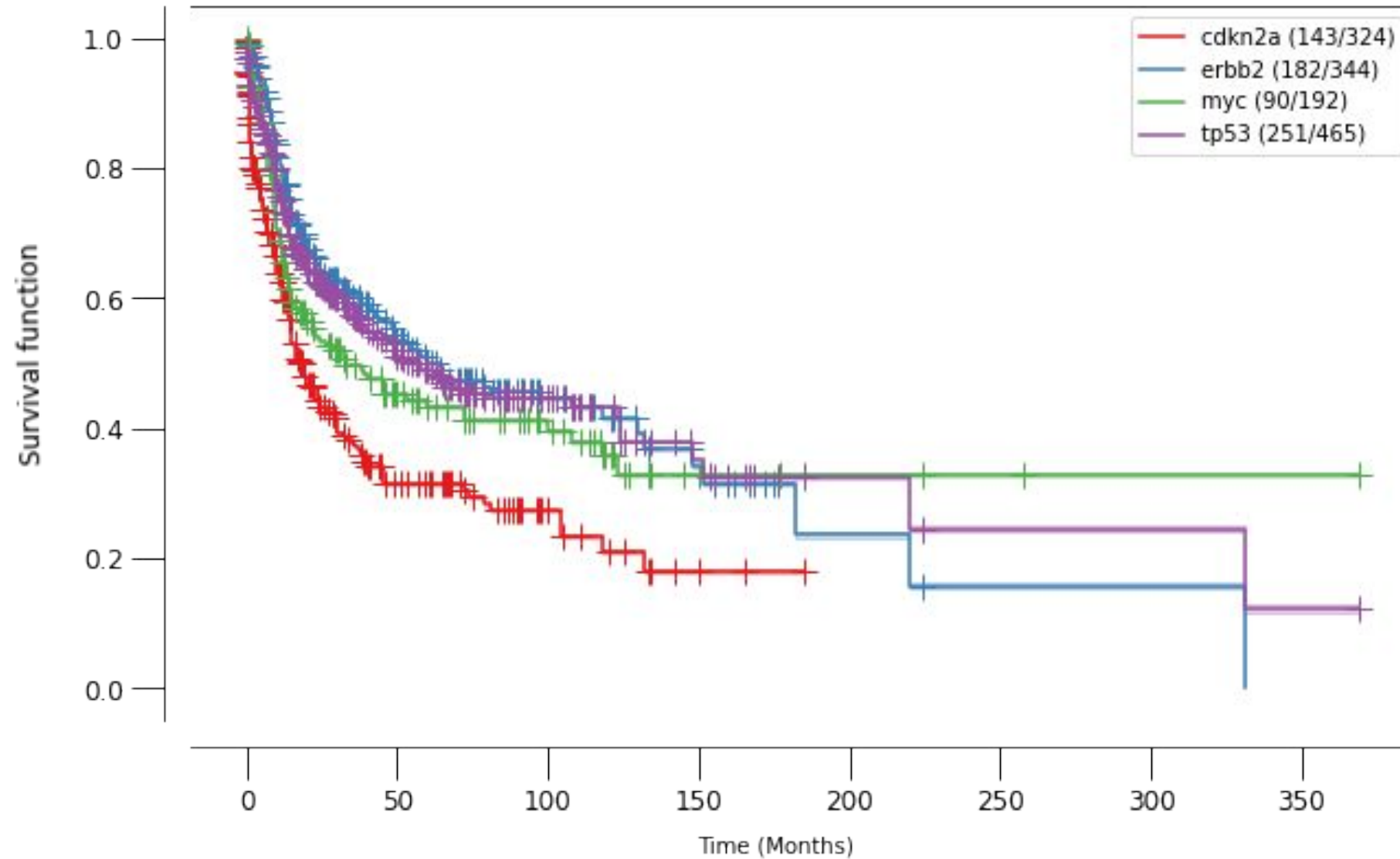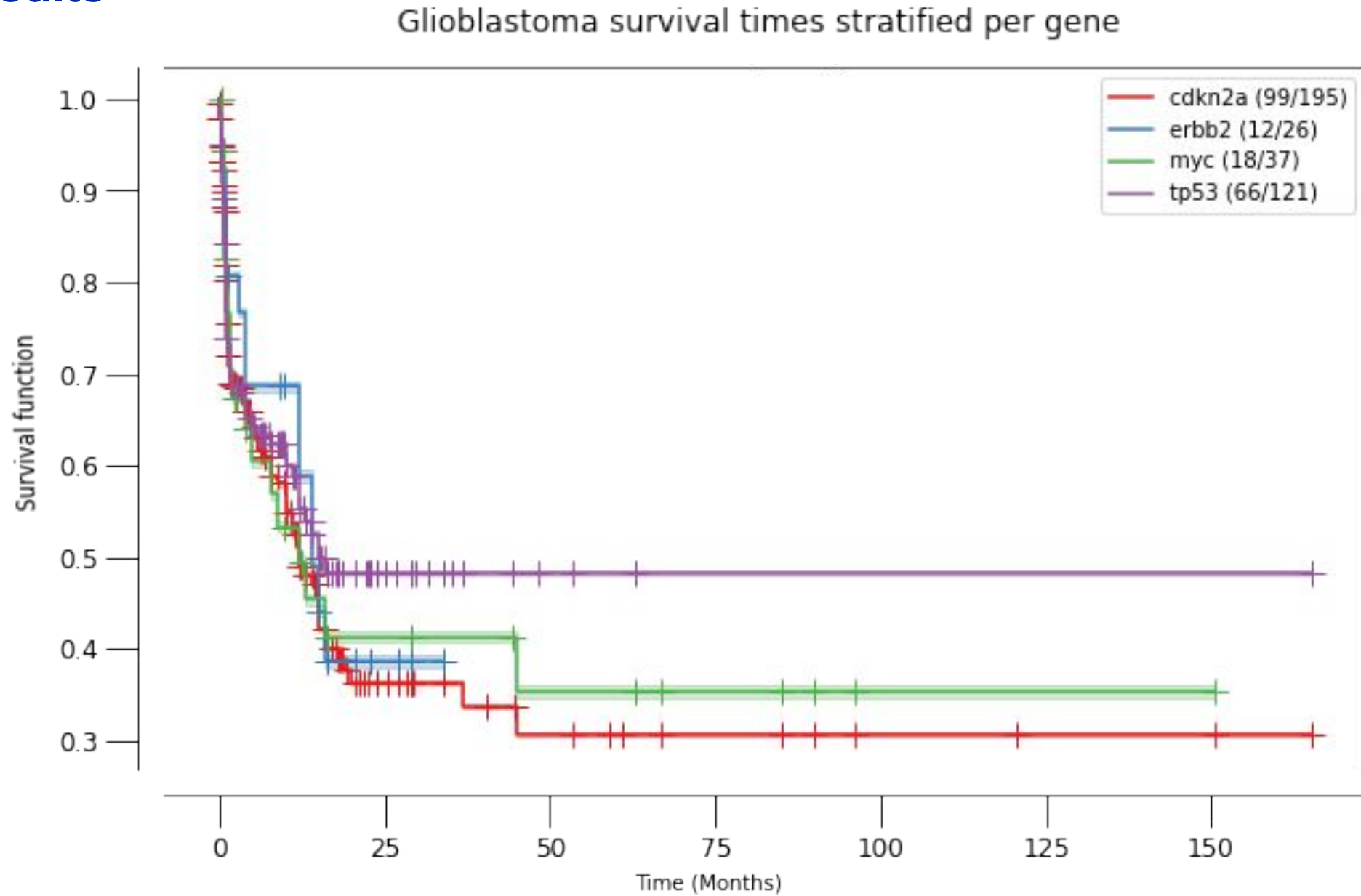
Results

Survival times for all cancers stratified per sex

Logrank P-Value = 0.62775

Conclusions

- Kaplan Meier Estimates:
    - p-value not calculated for the gene groups
    - Not significant for the sex:
        - No evidence against the null hypothesis that their hazard functions are identical

- Differences in survival time, visible in aggressive tumor types
- Survival time shortest with variations on cdkn2a
- No difference between male and female observations

Conclusions

- Limitations:
  - Age distribution very skewed
    - Kaplan Meier measures survival time after sample collection
    - might be different per age group
  - No reference group for the survival times

- Extensions:
  - Cox Regression for the survival times
    - add the covariates age and gene groups (factor variable)
    - gives either Hazard Ratios or Accelerated Failure Time

Sources

https://en.wikipedia.org/wiki/Logrank_test *(logrank test)*

https://www.msdmanuals.com/home/brain,-spinal-cord,-and-nerve-disorders/tumors-of-the-nervous-system/overview-of-brain-tumors *(classification of tumors)*

https://www.cancer.gov/types/brain/patient/adult-brain-treatment-pdq *(symptoms)*

https://progenetix.org/ *(data)*